

Neanderthal genome sees first light

Two research teams publish the first detailed glimpse of a Neanderthal genome this week, starting the race to unravel the genetic structure of modern man's closest relative. Articles in *Nature*¹ and *Science*² offer complementary yet contrasting views of nuclear DNA extracted from the same bone of a Neanderthal male who lived 38,000 years ago, found in a Croatian cave.

Both groups, which collaborated in part on their projects, say they need to sequence far more of the Neanderthal's DNA to answer key questions. But for now, the studies find roughly similar timescales for when Neanderthals and modern humans, *Homo sapiens*, diverged from each other in the course of evolution.

Given recent advances in DNA sequencing, a full Neanderthal genome could be sequenced within two years, the *Nature* authors say. "This is the golden age of ancient DNA work," says first author Richard Green, a postdoctoral researcher at the Max Planck Institute for Evolutionary Anthropology in Leipzig, Germany.

Neanderthals and *H. sapiens* roamed the same regions of Europe and western Asia until the Neanderthals went extinct 30,000 years ago. Both research groups now have genetic estimates for when the two species shared a most recent common ancestor.

In the *Science* article, team leader Edward Rubin places that event at roughly 706,000 years ago. In *Nature*, the Max Planck group — headed by palaeogeneticist Svante Pääbo — write that human and Neanderthal sequences diverged roughly 516,000 years ago. Within the large margins of error typical of such analyses, these conclusions could turn out to be the same. The *Nature* paper also takes a stab at estimating the size of the ancestral population that gave rise to humans and Neanderthals: roughly 3,000 individuals.

The gene studies may also shed light on a long-contested idea in palaeoanthropology: that Neanderthals and *H. sapiens* may have interbred. Last week, another research team proposed that modern humans acquired a version of the *microcephalin* gene — which regulates brain size — through interbreeding with another *Homo* species that has since gone extinct, possibly the Neanderthals³. Fossils — such as a 30,000-year-old skull from a Romanian cave⁴ — have also been put forward as evidence of hybridization between the two species.

The latest data suggest that some interbreed-



Sequencing of DNA from ancient bone might result in a full Neanderthal genome within two years.

ing may have taken place on a limited scale, says Pääbo. "One possibility is gene flow from modern human to Neanderthal," he says. But the data could also be explained if the studied Neanderthal sample was contaminated with modern human DNA. "We have contamination under control," Pääbo says.

As for the other group, "we don't see any evidence of interbreeding," says Rubin, director of the Joint Genome Institute (JGI) in Walnut Creek, California. "But we could have missed it because we don't have enough Neanderthal sequence yet."

Rubin's group reports analysis of about 65,000 base pairs. The *Nature* article reports about 1 million. The genomes of modern humans and Neanderthals each have about 3 billion base pairs. "These studies show you can do large-scale sequencing of Neanderthal DNA," says Jeffrey Wall, a computational biologist at the University of Southern California in Los Angeles who was not involved in either study. "There are some unresolved issues," he says. "In the end, the questions will be answered to everyone's satisfaction."

Both groups agree that less than 0.5% of the two species' genomes are different. But the teams largely used different sequencing methods. The JGI team opted for a traditional bacterial, or Sanger, method to replicate Neanderthal DNA. The Max Planck team used a newer, and faster, sequencing system⁵.

Both groups are pumping new sequences

into publicly accessible databases. Nearly 5 million base pairs are already available. By spring, Pääbo expects to have about 1% of the Neanderthal genome completed.

Rubin is now developing methods to target specific genes in the regions of the genome that are different in Neanderthals and modern humans. This approach, he says, allows one "to reach in and fish out DNA for analysis for different traits".

One of the first fishing trips will be for a gene called *FOXP2*, which in *H. sapiens* is linked to speech and language. Many animals have the gene, but the human version has distinct differences from that of the chimpanzee⁶.

Such genetic excursions will need more Neanderthal individuals for a truly representative picture of the differences between the species. Palaeoanthropologists and geneticists are now teaming up to acquire more bone, from more caves.

Eventually, genetics and palaeoanthropology will intertwine, predicts James Noonan, a JGI postdoc and first author on the *Science* article. "How biological features are encoded in the genome," he says, "will be correlated with what is seen in specimens."

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